



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/540,024	03/31/2000	Arthur O. Tzianabos	B0801/7169	1627

7590

03/10/2005

Helen C Lockhart
Wolf Greenfield & Sacks PC
600 Atlantic Avenue
Boston, MA 02210

EXAMINER

LIU, SAMUEL W

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/540,024

Applicant(s)

TZIANABOS ET AL.

Examiner

Samuel W Liu

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,6-19 and 149-165 is/are pending in the application.
- 4a) Of the above claim(s) none is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6-19 and 149-165 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of claims

Claims 1, 6-19 and 149-165 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/24/05 has been entered. Also, Applicant's amendment filed 1/24/05, which cancels claims 2-5 and 20-148, amends claims 8-13, 19, 149-157 and 163, and adds claims 164-165, has been entered.

The following Office action is applied to the pending claims 1, 6-19 and 149-165.

Claim Rejections - 35 USC §112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1, 6-19 and 149-165 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is not apparent in the recitation "composed of ... amino moiety and a negative charge" because said "negative charge" does not conform to said "amino moiety", as is noted that the negative charge has a general meaning that a surplus of electrons or a lower electric potential. Does the "negative charge" refer to *net* negative charge of the entire charge moiety, or

Art Unit: 1653

a negatively charged of a particular chemical moiety? See also claims 19 and 152-154. The dependent claims are also rejected.

Claim 15 recites “non-native polypeptide”; the recitation is unclear because “non-native” ambiguously refers to (i) a denatured form of said polypeptide which structurally and functionally differs from the native form of the polypeptide; or (ii) a recombinantly produced or chemically modified polypeptide. Which one is it? Note that the specification does not define this recitation.

Claim 16 is indefinite in the recitation “... a polypeptide having at least one modified amino acid” because without setting forth polypeptide sequence with sequence identifier, one is unable to make said modification to the polypeptide so as to maintain the claimed polymer to consist of identical repeating units. See also claims 17 and 160-161.

Claim 8 recites “10 charge motif”; the recitation is not apparent because claim 1 from which claim 8 depends sets forth that each repeating unit has only one charge motif; are said “10 charge motifs” in fact equal to the 10 repeating units? See also claims 9-10 and 149-151.

Claim 154 recites “... are on adjacent amino acids”; the recitation appears to be awkward as to whether or not adjacent amino acids refers to proximity of the amino acids in view of primary structure, or proximity in view of tertiary structure (protein folding). Note that the specification does not define “adjacent amino acids” thereof.

Claim 164 recites “the polypeptide consists of (K-D)_n”; there is insufficient antecedent basis for this limitation in claim 19 from which claim 164 depends. The said recitation does not

Art Unit: 1653

appear to conform to the claim 19 limitation “*the positively charged free amino moiety of the charge motifs is separated by a distance of at least 8 amino acids from the positively charged amino moiety of another charge motif*”; i.e., the limitation of “(K-D)_n” of claim 164 is out of the scope set forth in claim 19. See also claim 165.

The applicants' response to the rejection under 35 USC, second paragraph

On page 10, the 3rd paragraph, the response filed 1/24/05 asserts that the recitation “non-native polymer” can be understood with respect to “non-native polypeptide” and that the specification has defined “polymer”; and the response submits that the recitation is clearly referred to a polypeptide which differs in composition and sequence from naturally occurring polypeptides and could be prepared by isolation from natural source without further modification. Thus, the applicants infer that the recitation is not unclear (see page 11, the 1st paragraph). The applicants' argument has been fully considered but is found to be unpersuasive because (i) the specification does not define the non-native polypeptide; (ii) the definition of “polymer” in the instant specification cannot substitute for the definition of the non-native polymer; and (iii) said non-native polymer encompasses denatured form of said polymer, e.g., polypeptide, wherein the denatured polymer (polypeptide) can be a product isolated from natural source without further chemical modification.

On page 11, the response further argues that the phrase “adjacent amino acids” is not unclear as the specification has implied that “adjacent” refers to proximity of amino acid residues within primary structure (*not tertiary structure*) of the claimed composition. The applicants' argument is found to be unpersuasive because claim 154 is directed to a polypeptide of molecular weight about 50 KDa which has tertiary structure, absent the factual indicia to the

Art Unit: 1653

contrary. Hence, the "adjacent amino acids" would encompass (i) the amino acids which are in neighboring within foled polypeptide and (ii) the amino acids adjacent in primary protein struture thereof. Yet, the specification does not make it clear in this regard.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The claims 1, 8-10, 14-16, 18-19, 149-151, 154, 158-160 and 162-163 are rejected under 35 U.S.C. 102(b) as being anticipated by Arnot, D. E. et al. (US Pat. No.5700906).

In the patent claim 1, Arnot et al. discloses a peptide of amino acid sequence that consists of the sequence (DRAAGQPAG)_n wherein n is between 2 and 18. The said peptide has structural features: (i) the peptide consists of repetitive units (2-18); (ii) molecular weight of the peptide

Art Unit: 1653

has less than 50 KDa; (iii) each unit has a charge motif, i.e., "DR" which consists of a positively charged arginine (R) and a negatively charged aspartic acid (D); (iv) any two positively charged arginine residues are separated by 8 amino acid residues, i.e., at least 32 Å distance (*in view of that a dimension occupied by 8 amino acid residues is equivalent to 32 Å* (see page 21, lines 24-25 of the specification)); and (v) the charged motifs are separated by neutral units "AAGQPAG". The above-stated structural features meet the limitations set forth in claims 1 and 19. On column 10, lines 61-67, Arnot et al. further teach a pharmaceutical (vaccine) composition comprising said peptide. Thus, the Arnot's disclosure anticipates the instant claims 1 and 19.

The Arnot's peptide consists of at least 10 charge motifs, which anticipates the instant claims 8 and 149.

The Arnot's peptide consist of at least 15 charge motifs, which anticipates the instant claims 9 and 150.

In the patent claim 3, Arnot at al. teach that the parameter "*n*" is larger than 19, i.e., the peptide has at least 20 charge motifs, which anticipates the instant claims 10 and 151.

In the patent claim 2, Arnot at al. teach that the peptide is chemically synthesized, which anticipates the instant claims 14-15 and 158-159.

On column 10, lines 43-47, Arnot et al. teach that the synthetic peptide is modified so as to be linked to other composition. For doing so, within said peptide at least one amino acid must be subject to the modification. Thus, the above Arnot' teaching anticipates the instant claims 16 and 160.

Art Unit: 1653

In the Arnot' peptide, the ratio of a positive (R) to negative (D) charge ratio is of 1:1, which anticipates the instant claims 18 and 162.

In the Arnot's peptide, the positively charged arginine is not separated from negatively charged aspartic acid, i.e., they are adjacent, which anticipates the instant claim 154.

In the Arnot's peptide, the charged motifs are separated by neutral amino acids "AAGQPAG", which anticipates the instant claim 163.

The claims 1, 6 and 8-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Mayes, A. E. et al. (US Pat. No.6150459).

In Example 1, Mayes et al. a copolymer (molecular weight about 40 KDa) consisting of identical repeating units; each of said unit consists of ethylene-oxide monomer unit $[-(\text{CH}_2-\text{CH}_2-\text{O})_n-]$ of polyethylene glycol (PEG) and a charge motif, i.e., GRGDSP, that consists of a positively charged arginine (R) and a negatively charged aspartic acid (D); wherein "GRGDSP" peptide is conjugated (covalently) to the PEG monomer unit by trsyl chloride chemistry (see column 18, lines 39-42). The Mayes' copolymer has the following additionally structural characteristics: (i) within said charge motif, the two positively charged arginine (R) residues are separated by 8 amino acids plus the said PEG monomer unit(s), i.e., at least 32 Å distance; and, (ii) the charged motifs (RGD) are separated by neutral units, e.g., "SP-[PEG- monomer unit(s)]-G". The Mayes' copolymer meets the all limitations set forth in the claimed polymer of claims 1 and 19. Additionally, Mayes et al. teach the copolymer can be formulated as a therapeutic composition for drug delivery (see column 17, the 3rd paragraph). The above the Mayes' teachings therefore anticipate the instant claim 1.

Art Unit: 1653

In Example 1, Mayes teach that the copolymer is chemically synthesized as a mixed polymer (i.e., chemical homopolymer PEG and biopolymer "GRGDSP" peptides), which anticipates the instant claim 6.

In Example 1, Mayes et al. teach that at least 5 wt % conjugates (i.e., "GRGDSP" charge motifs) are linked to the PEG mother chain mediated by trsyl chloride, and that the resultant copolymer has molecular weight of ~ 40 KDa. Said 5 wt % conjugates would results in approximately 45 "GRGDSP" peptide conjugates in the copolymer (the calculation is as follows: $40000/44 \times 5\% \approx 45$, wherein the PEG monomer $[-(\text{CH}_2-\text{CH}_2-\text{O})-]$ has molecular weight ~ 44, see the attachment cited in the item "V" of PTO-892). Hence, the Mayes' copolymer has more than 20 charge motifs, i.e., "GRGDSP" sequences. The Mayes' teaching anticipates the instant claims 8-10.

Considering the fact that the rest 95% (out of 5 wt %) of the monomer units of PEG remain unmodified with "GRGDSP" sequences, and considering that the conjugation of the sequences (i.e., the charge motifs) to the PEG polymer are unevenly/evenly distributed within the copolymer, there is at least two positively charged moieties (side chains of arginine residues) are separated from each other by a distance of at least 200 Å. This anticipates the instant claims 11-13.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach

Art Unit: 1653

the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.



Samuel Wei Liu, Ph.D.
Art Unit 1653, Examiner
March 1, 2005



KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER